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EXAMINER	
KAROL, JODY LYNN	

ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,735	STEIGER, MICHEL	
	Examiner	Art Unit	
	Jody L. Karol	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-23,25-32,35 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-23,25-32,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/14/2009 has been entered.

The Notice of Non-Compliant Amendment sent out on 2/5/2009 is herein withdrawn (see remarks *infra*) and the Amendments to the claims filed 1/15/2009 have been entered into the Application. Claims 15-19 and 32 have been amended. Claims 1-14, 24, and 33-34 are cancelled. Claims 35-36 are newly added. Thus, claims 15-23, 25-32, and 35-36 are pending and are currently under consideration.

WITHDRAWN REJECTIONS

1. In view of Applicant's amendment to claim 32 and cancellation of claims 33-34, the objection to claims 32-34 is herein withdrawn.

2. In view of Applicant's amendment to claim 32 and cancellation of claims 33-34, the rejection of claims 32-34 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is herein withdrawn.

3. In view of Applicant's amendment to claims 15-19, the rejection of claims 15-23 and 25-30 under 35 U.S.C. 112, first paragraph, for scope of enablement, is herein withdrawn.

4. In view of Applicant's amendment to claim 32 and cancellation of claims 33-34, the rejection of claims 32-34 under 35 U.S.C. 112, 2nd paragraph, as being indefinite, is herein withdrawn.

Response to Arguments

5. Applicant's arguments filed 5/14/2009 have been fully considered but they are not persuasive.

Applicant argues that the Notice of Non-Compliant Amendment was in error because claim 34 was present in the Amendment dated April 29, 2008. The Notice of Non-Compliant Amendment sent out on 2/5/2009 is herein withdrawn. As Applicant noted, claim 34 appears on top of page 6 of the Amendment dated April 29, 2008. However, it is noted that this claim appears on the same page as the amended abstract, and thus the abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). Thus, the specification is objected to as described *infra*, for failure to submit the abstract separately.

Applicant alleges that the refusal to enter the Amendment of January 13, 2009 is improper because the Amendment: 1) raised no new issues; 2) did not present additional claims without cancellation of a corresponding number of finally rejected

claims; 3) did place the case in condition for allowance; and 4) did reduce the number of issues on appeal. In response it is respectfully submitted that amended claim 32 and new claims 35-36 raise new issues that would require further search and consideration. Claims 32, and now-cancelled claims 33-34 were examined based upon the recitation that the composition contained 0.010% (w/w) diclofenac sodium. Further search and consideration is required for claims 32 and 35-36, directed to compositions containing 0.1% (w/w) diclofenac sodium with components not required by the other pending claims, such as benzyl alcohol, coco-caprylate/caprate, or compositions without a C_{2-4} alkanol.

Applicants further alleges that the recitation of 0.01% in claims 32 was clearly a typographical error, especially in view of Applicant's statement on page 8 of the Amendment dated August 13, 2008 that 0.1% is the minimal effective concentration. This is not found persuasive because several of the other claims (i.e. claim 15) were directed to compositions containing less that 0.1% (w/w) diclofenac sodium Thus, it is not clear that the recitation of 0.01% (w/w) diclofenac sodium was in error because similarly, other claims were directed to concentrations of diclofenac sodium (i.e. 0.02% (w/w)) below the admitted minimum effective concentration.

Applicant argues that the Examiner's citation of *In re Susi* is in the form of a *per se* rule, i.e. that a broad teaching in the art inherently supports the obviousness rejection of a claim to a narrower invention, but that there is no such *per se* rule. The Applicant states that to rely on Asche et al, the Examiner must find motivation or suggestion in the teaching to one of ordinary skill in the art to make the claimed

invention. In response it is respectfully submitted that the purpose of the citation of *In re Susi* was to rebut Applicant's arguments that Asche et al. does not teach 0.1% sodium diclofenac. While Asche et al. does not explicitly teach 0.1% sodium diclofenac, it is clearly contemplated by the teachings of Asche et al. (see abstract). Further, Betlach et al. (US 5,374,661) teach similar compositions comprising 0.1% sodium diclofenac solubilized with water, a glycol and an alcohol (see abstract; column 4, lines 24-27). Additionally, the substitution of acceptable alternatives for the specific components in the examples taught by Asche et al. (i.e. ammonia for triethanolamine) is considered to be obvious because the prior art specifically teaches them as acceptable alternatives.

It is recognized that the specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. *Corning Glass Works v. Sumitomo Elec.*, 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables (i.e. ammonia as the basic agent instead of triethanolamine in the composition comprising sodium diclofenac), anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR v. Teleflex*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. A.G. Pro*, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant

question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (*Id.*). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR v. Teleflex*, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is... a person of ordinary creativity, not an automaton." *Id.* at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients (i.e. ammonia as a basic agent instead of triethanolamine) from within a prior art disclosure, to arrive at compositions "yielding no more than one would expect from such an arrangement," i.e., for ammonia to act as a base.

Lastly, Applicant argues that the Examiner has ignored the narrowing language of claims 17-19, 31-32, and 35-36. In response it is respectfully submitted the narrowing claim language has been taken into consideration. However, the compositions taught by Asche et al. do not require any components that are prohibited by the narrowing language of claims 17-19, 31-32, and 35-36, aside from claims 35-36 wherein the C_{2-4} alkanol is excluded. However, this exclusion has been addressed in the new ground(s) of rejection presented below. Thus, it is unclear as to what teaching in the cited prior art violates the narrowing claim language.

Thus, for these reasons, Applicant's arguments are found unpersuasive. The claims are still considered properly rejected under 35 U.S.C. 103(a) and thus, said rejection is maintained.

REJECTIONS

6. The following rejections and/or objections are either reiterated from the previous Office Action dated 8/19/2008 or newly applied. They constitute the complete set of rejections and/or objections presently being applied in the instant application.

Specification

7. The abstract of the disclosure is objected to because the abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 15-23 and 25-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asche et al. (US 4,917,886).

The instant claims are directed to a pharmaceutical composition for topical use, wherein the composition is an opaque emulsion-gel, is completely devoid of an anti-fungal drug, and comprises diclofenac sodium salt, water, at least one C_2-C_4 alkanol, a glycol solvent selected from the group consisting of propylene glycol and polyethylene glycol (200-20,000), at least one gelling agent selected from the group consisting of carbomers, at least one lipid, at least one nonionic surfactant, and a basic agent selected from the group consisting of ammonia, sodium hydroxide, potassium hydroxide to adjust the pH of the total composition to 6.5-8. It is noted that component (c) may or not be present because the range encompasses zero.

Claims 15-16, 20-23, 25, and 27-30 are interpreted as broad and open-end by virtue of the term "comprising." Claims 17-1and 31 are limited by the phrase "consists essentially of," which limits the scope of the claims to the specified materials or steps "and those that do not affect the basic and novel characteristic(s)" of the claimed

invention. *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976). However, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355. Claim 19, 32 and 35-36 are interpreted as closed-ended by virtue of the phrase "consists of."

Asche et al. teaches topical compositions containing the following components in the following approximate ranges (see abstract):

i. 0.1-10% by weight of an anti-inflammatory active compound having at least one acidic group, such as diclofenac sodium as claimed in the instant claims 15-23, 25-32 and 35-36 (see column 7, lines 45-54);

ii. 10-50% by weight of a C_2-C_4 alkanol as claimed in the instant claims 15, 17, 20-23, and 26-31, such as ethanol or especially isopropanol, or mixtures thereof, as claimed in the instant claims 16, 18, 25, and 32 (see column 3, lines 58-62);

iii. 3-50% by weight of a lipid or mixture of lipids as claimed in the instant claims 15-26 and 29-31, such as paraffins, isopropyl myristate, or fatty acid esters such as caprylic/capric acid esters of fatty alcohols having 12 to 18 carbons, among several others as claimed in the instant claims 27-28 (see columns 4-5, and specifically column 4, line 22, and column 5, lines 17-31);

iv. 0.5-2% by weight of a gel structure former (gelling agent), such as polyacrylate (carbomer) as claimed in the instant claims 15-23, 25, 27-33,

and 35-36 (see column 7, lines 5-14), and specifically acrylic acid polymerisate, Carbopol® 934 P, which is analogous to carbomer 934 as claimed in the instant claim 26 (see column 2, line 57 to column 3, line 7);

v. 1-20% by weight of a co-solvent, such as polyethylene glycol (200-6,000) or propylene glycol (200-6,000 units) as claimed in the instant claims 15-23, 25-32, and 3-36 (see column 3, line 66 to column 4, line 7);

vi. 40-80% by weight of water as claimed in the instant claims 15-23, 25-32, and 35-36;

vii. 0.5-5% by weight of an emulsifier provided the lipid phase is not self-emulsifying, such as a non-ionogenic (nonionic) surfactant as claimed in the instant claims 15-28 and 30-31 (see column 5, lines 54-56), specifically polyethylene ethers of fatty alcohols having 2 to 23 ethylene oxide units as claimed in the instant claim 29, (see column 6, lines 23-27); and

viii. optionally non-essential constituents, for example bases such as sodium salts, potassium salts, and ammonia as claimed in the instant claims 15-23, 25-32, and 35-36 (see column 9, lines 1-5, and column 7, lines 51-57).

wherein the composition has a pH of approximately 5 to approximately 7.5, and combines the properties of a gel and an oil/water emulsion (see column 1, lines 30-61). Asche et al. further teaches that a base may be essential for neutralizing the acidic groups of the active ingredients and the gel structure formers (i.e. carbomers), and adjusting the pH of the composition (see column 9, lines 1-9). Additional components

such as chemical stabilizers may or may not be present as claimed in the instant claim 30 (see column 8, lines 35-39). Anti-fungal agents are not listed as a possible optional constituent.

Asche et al. does not teach a specific example where the components are within the claimed ranges. However, it would have been obvious to one of ordinary skill at the time of the invention to utilize the teachings of Asche et al. to formulate the claimed compositions. In this case, where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976).

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

10. Claims 32 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asche et al. (4,917,886) as applied to claims 15-23 and 25-31 above, in view of Levine et al. (US 6,126,959) and Betlach, II (US 5,374,661).

The instant claims 32 and 35-36 are directed to specific pharmaceutical formulations in the form of an emulsion gel for topical use containing 0.1% (w/w) diclofenac sodium salt. Claim 32 additionally consists of 76.5% (w/w) water, 10.0% (w/w) isopropanol, 5.0% (w/w) propylene glycol, 0.7% (w/w) Carbomer 980, 2.5% (w/w) liquid paraffin, 2.5% (w/w) coco-caprylate/caprate, 2.0% (w/w) polyoxyethylene-20-cetostearyl ether, and 0.63% (w/w) ammonia, concentrated solution in water. Claim 35 additionally consists of 74.9% (w/w) water, 15.0% (w/w) propylene glycol, 1.0% (w/w)

Carbomer 974P, 2.5% (w/w) liquid paraffin, 2.5% (w/w) coco-caprylate/caprate, 2.0% (w/w) polyoxyethylene-20-cetostearyl ether, 1.5% (w/w) 30% aqueous NaOH solution, and 0.5% (w/w) benzyl alcohol. Claim 36 additionally consists of 86.68% (w/w) water, 5.0% (w/w) propylene glycol, 0.3% (w/w) Carbomer 974P, 2.5% (w/w) liquid paraffin, 2.5% (w/w) coco-caprylate/caprate, 2.0% (w/w) polyoxyethylene-20-cetostearyl ether, 0.42% (w/w) 30% aqueous NaOH solution, and 0.5% (w/w) benzyl alcohol.

Asche et al. is described *supra* as applied to claims 15-23 and 25-31. Asche et al. further teach that the lipid or mixture of lipids include fatty acid esters such as caprylic/capric acid esters of fatty alcohols having 12 to 18 carbons, i.e. Cetiol® LC (coco-caprylate/caprate) as claimed in the instant claims 32 and 35-36 (see column 5, lines 29-31). Asche et al. also teach specific polyethylene ethers of fatty alcohols having 2 to 23 ethylene oxide units include polyhydroxyethylene cetyl stearyl ether, encompassing the polyoxylethylen-20-cetostearyl ether as claimed in the instant claims 32 and 35-36 (see column 6, lines 32-36).

Asche et al. do not teach Carbomer 980 as claimed in the instant claim 32, or Carbomer 974P as claimed in the instant claims 35-36. Asche et al. do not teach compositions without a C_{2-4} alkanol and with benzyl alcohol as claimed in the instant claims 35-36. Asche et al. do not teach 30% aqueous NaOH solution as claimed in the instant claims 35-36. Asche et al. do not exemplify a composition with the requisite concentrations of components as claimed.

Levine et al. teach carbomers are gel formers, and that Carbopol 934P can be substituted by other gel formers included Carbomer 974P or Carbomer 980 *inter alia* (see column 7, lines 64-67).

Betlach, II teaches a topical drug delivery composition comprising diclofenac sodium, wherein the diclofenac sodium is solubilized in a mixture of water, a lower molecular weight alcohol, and a glycol (see abstract). Betlach, II teaches the concentration of diclofenac is between approximately 0.1% to 2.5% (see column 4, lines 24-27). Betlach, II further teach that preferred glycols include propylene glycol, wherein the amount of glycol is approximately between 0.5% and 20% (see column 4, lines 28-37), and lower molecular weight alcohols include isopropyl alcohol (isopropanol) and benzyl alcohol, wherein the amount of alcohol is high enough to solubilize the diclofenac, i.e. 1 to 50% (w/w) (see column 4, lines 44-54).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute one of the carbomers taught by Levine et al. in the diclofenac composition obvious over Asche et al. One of ordinary skill in the art would have been motivated to select a different carbomer with a reasonable expectation of success because the carbomers are taught by Levine et al. to be equivalent gel formers. The selection of a known material based on its suitability for its intended use supported a *prima facie* obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945).

It would have been obvious to one of ordinary skill in the art at the time of the invention to utilize benzyl alcohol as taught by Betlach, II instead of isopropanol in the

composition obvious over Asche et al. One of ordinary skill in the art would have been motivated to use benzyl alcohol instead of isopropanol because it is taught by Levine et al. to solubilize diclofenac sodium. One of ordinary skill in the art would have had a reasonable expectation of success in employing benzyl alcohol instead of isopropanol because like Asche et al., Betlach, II teach a composition comprising a similar concentration of diclofenac solubilized by a glycol such as propylene glycol, an alcohol such as benzyl alcohol, and water. Thus, a combination of benzyl alcohol, water, and propylene glycol is expected to maintain the solubility of the diclofenac in the formulation obvious over Asche et al.

In regards to claims 35-36, while the prior art references do not explicitly teach 30% aqueous NaOH, Asche et al. teach basic Na salts for adjusting the pH (see column 9, lines 1-9). NaOH is a well known basic Na salt for adjusting the pH, and the optimization of the amount in an aqueous solution is well within the purview of the ordinary artisan.

In regards to the requisite concentrations of the components as claimed, while the prior art references do not exemplify the specific concentrations, the claimed ranges lie within the ranges disclosed by the prior art, or are close to the ranges disclosed by the prior art. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 U.S.P.Q. 223, 235 (C.C.P.A. 1955). Thus, the determination of optimal or workable amounts of the components by routine experimentation is obvious absent showing of criticality of the claimed amounts. One

having ordinary skill in the art would have been motivated to do this to obtain an emulsion-gel containing sodium diclofenac for topical administration.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time it was made.

Conclusion

No claims are allowed.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jody L. Karol whose telephone number is (571)270-3283. The examiner can normally be reached on 8:30 am - 5:00 pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Jody L. Karol/

Examiner, Art Unit 1617

/JENNIFER M KIM/
Primary Examiner, Art Unit 1617